synthesizing cDNA of said abundant expressed genes in said RNA sample;

removing said abundant expressed genes [hybridized with the probes] in RNA sample; and

recovering said rare expressed genes [not hybridized with the probes] of synthesized cDNA.

Please add the following new claim 28:

--28. (New) A method for preparation of RNA sample according to claim 22, wherein said region hybridized with said probes is digested by Ribonuclease H.--

REMARKS

Reconsideration of this application is respectfully requested. Claims 22, 23, and 28 are pending in the application, with claims 22 and 23 having been amended and new claim 28 having been added.

Claims 22 and 23 have been rejected under 35 U.S.C. 102(b) as being anticipated by Lee et al. (*Proc. Nat'l. Acad. Sci. 88*:2825-2829 (April, 1991)).

Claims 22 and 23 have also been rejected under 35 U.S.C. 102(b) as being anticipated by Hedrick et al. (*Nature 308*:149-153 (March, 1984)).

Claims 22 and 23 have been amended in order to clarify the distinctive feature of the present invention and new claim 28, dependent upon claim 22, has been added. The amendment of claim 22 is supported in the embodiment 1, Figure 2A through Figure 4E (please refer the description of the specification on page 9, line 10 to page 16, line 15). The amendment of claim 23 is supported in the embodiment 2, Figure 5A through Figure 5G (please refer the description of the specification on page 16, line 16 to page 18, line 20).

According to amended claim 22, abundant expressed genes hybridized with probes are digested at a region hybridized with said probes and oligo dT primers are added in order to synthesize cDNA of rare expressed genes in an RNA sample so that the rare expressed genes are effectively recovered.

According to amended claim 23, the known sequences of abundant expressed genes are hybridized with probes and oligo dT primers are added in an RNA sample in order to synthesize cDNA of rare expressed genes, while said probes prevent synthesizing cDNA of abundant expressed genes in the RNA sample. Therefore, rare expressed genes are effectively recovered.

Lee at al disclose "cDNA-RNA hybridization distinguishes mRNAs that are equally expressed in both parental cell lines from those unpairad cDNAs that are uniquely expressed in the

parental cells of interest" (refer, page 2825, 2nd column, 3rd paragraph), and normal cDNA is hybridized with mRNA of a tumor in the first subtraction (refer, Fig.1 and page 2826, 2nd column, 3rd paragraph).

However, Lee et al only disclose that mRNA uniquely expressed to one parental cell is subtracted. Lee et al never disclose or suggest that abundant expressed genes hybridized with probes are digested at a region hybridized with probes and that cDNA of rare expressed genes in an RNA sample is synthesized by adding oligo dT primers (claim 22). Further, Lee et al never disclose or suggest that synthesizing cDNA of abundant expressed genes in an RNA sample is prevented by probes and that cDNA of rare expressed genes is synthesized by adding oligo dT primers (claim 23).

Hedrick et al. disclose analyzing the kinetics of cDNA-mRNA hybridization reaction, wherein cDNA from polysomal RNA is repeatedly hybridized to B-cell mRNA (refer, page149, 2nd thorough page150, 2nd column) .

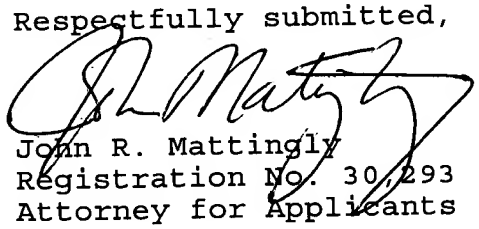
However, Hedrick et al never disclose or suggest that abundant expressed genes hybridized with probes are digested at a region hybridized with probes and that cDNA of rare expressed genes in an RNA example is synthesized by adding oligo dT primers (claim 22). Further, Lee et al. never disclose or suggest that synthesizing cDNA of abundant

expressed genes in an RNA sample is prevented by probes and that cDNA of rare expressed genes is synthesized by adding oligo dT primers (claim 23).

Accordingly, it is requested that the rejections of claims 22 and 23 under 35 U.S.C. 102(b) as being anticipated by Lee et al. and Hedrick et al. be withdrawn.

In view of the foregoing, it is submitted that this application is now in condition for allowance and an early Office Action to that end is earnestly solicited.

Respectfully submitted,



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VERSION WITH MARKINGS TO SHOW CHANGES MADE

22. (Amended) A method for the preparation of an RNA sample including rare expressed genes, comprising the steps of:

[(1) hybridizing an] providing an RNA sample having [one or plural] abundant expressed genes and rare expressed genes [with probes], said abundant expressed genes each having a known sequence[,];

[said] adding probes [hybridizing] to hybridize specifically with the known sequences of said abundant expressed genes;

digesting a region hybridized with said probes in said abundant expressed genes;

removing said probes;

adding oligo dT primers to synthesize cDNA of said rare expressed genes in RNA sample;

removing said abundant expressed genes in said RNA sample; and

[(2)] recovering said rare expressed genes [not hybridized with the probes] of synthesized cDNA.

23. (Amended) A method for the preparation of an RNA sample including rare expressed genes, comprising the steps of:

[(1) hybridizing an] providing an RNA sample having [one or plural] abundant expressed genes and rare expressed genes [with probes], said abundant expressed genes each having a known sequence[,];

[said] adding probes [hybridizing] to hybridize specifically with the known sequences of said abundant expressed genes;

adding oligo dT primers to synthesize cDNA of said rare expressed genes in said RNA sample, while said probes prevent synthesizing cDNA of said abundant expressed genes in said RNA sample;

[(2)] removing said abundant expressed genes [hybridized with the probes] in RNA sample; and

[(3)] recovering said rare expressed genes [not hybridized with the probes] of synthesized cDNA.